REMARKS

This is in response to the Office Action of November 13, 2007. Claims 39-44, 47-55, and 57-65 are cancelled, without prejudice. Claims 37, 45, and 46 are reduced in scope. No new matter has been introduced. Claims 37, 38, 45, 46, and 56 are pending in this application.

Prior art rejections

Claims 37-40, 44-46, and 56 were rejected under 35 U.S.C. § 103(a) as being unpatentable over WO 97/20899 (Mitch) or WO 96/12711 (Merritt) or US 5,512,574 (Husbands) or US 5,888,999 (Bodick) and EP 555,478 (Chokai) in view of US 5,948,793 (Abreo). Office action, pages 2-8. The rejections – to the extent that they might be applied against the claims of reduced scope presented herein – are respectfully traversed.

Mitch and Merritt and Husbands and Bodick and Chokai and Abreo all fail to describe the azabicyclo[2.2.2]octyloxy-pyridazine compounds of the present invention. Neither Mitch nor Merritt nor Husbands nor Bodick nor Chokai reports activity as nicotinic acetylcholine receptor agonists. The Examiner refers to position isomerism in support of the rejection. Although position isomerism is a fact of a close structural similarity, position isomerism is not necessarily an indication of a similar biological activity, as may be seen for instance by reference to Exhibits 1 and 2 enclosed herewith.

Exhibit 1 shows a comparative study of the nicotinic activity of some position isomeric pyridyl-homopiperazines. While the 2-pyridyl- and 4-pyridyl-homopiperazines are both virtually inactive, the 3-pyridyl-homopiperazines show a potency of a factor 2000 or more.

Exhibit 2 demonstrates the same effect. Exhibit 2 shows a comparative sturdy of the nicotinic activity of some position isomeric azabicyclooctane-oxy-pridazines/pyrimidines. Here the azabicyclooctane-oxy-pyridazine is about 10 times more potent compared to the azabicyclooctane-oxy-pyrimidine.

There is, therefore, no general rule that position isomers share their biological activities – in fact, Exhibits 1 and 2 demonstrate that the contrary is the case.

While the present invention is concerned with providing new nicotinic agents, Mitch and Merritt and Husbands and Bodick and Chokai – the references relating to "position isomers" –

teach only muscarinic activity. There is absolutely no indication of an activity at the nicotinic receptors. Accordingly, these references provide no motivation to persons of ordinary skill in the art to alter the muscarinic compounds described by Mitch and Merritt and Husbands and Bodick and Chokai in the expectation of obtaining the nicotinic compounds of the present invention.

The Abreo reference does not make up for this deficiency in the primary references. While Abreo describes compounds showing a nicotinic activity, the Abreo compounds have no resemblance to the compounds of the present invention. Thus the Abreo reference provides no motivation to the person of ordinary skill in the art to alter the Abreo compounds in the expectation of obtaining the nicotinic compounds of the present invention.

Withdrawal of all prior art rejections of record is in order and is earnestly solicited.

Double patenting rejections

Claims 37-40, 44-46, and 56 were provisionally rejected on the ground of obviousness-type double patenting over claims 1-7, 11-20, and 29 of later-filed application Serial No. 10/591,871. Office Action, page 9. The rejection is respectfully traversed. SN 10/591,871 describes azabicyclo[2.2.2]octyl-carboxylic acid amides of a complex and more remote chemical structure compared to the azabicyclo[2.2.2]octyloxy-pyridazine compounds of the present invention.

Claims 37-40, 44-46, and 56 were provisionally rejected on the ground of obviousness-type double patenting over claims 1-11, 13-21, and 23 of later-filed application Serial No. 11/663,152. Office Action, page 9. The rejection is respectfully traversed. SN 10/663,152 describes azabicyclo[2.2.2]octyloxy-pyridazinyl-ethynyl-phenyl derivatives that have a quire distinct substitution pattern (phenyl-ethynyl) on the pyridazinyl group compared to the azabicyclo[2.2.2]octyloxy-pyridazine compounds of the present invention.

Contact information

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Richard Gallagher (Reg. No.

28,781) at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37.C.F.R. §§1.16 or 1.14; particularly, extension of time fees.

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Respectfully submitted,

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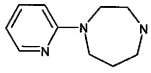
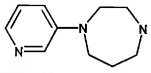
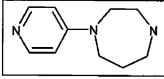
MAA/RG

Exhibit 1

Comparative studies of position isomeric pyridyl-homopiperazines

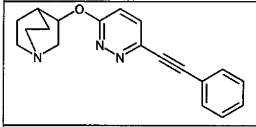
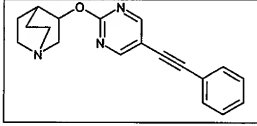
Structure	Affinity* (IC_{50}; μM)
	32
	0.0046
	11

*) *In vitro* inhibition of ^{3}H-epibatidin binding, tested as described in e.g. US 6,756,386, column 10.

Exhibit 2

Comparative studies of position isomeric

azabicyclooctane-oxy-pyridazines/pyrimidines

Structure	Affinity* (IC_{50}; µM)
	0.7
	6.0

*) *In vitro* inhibition of ^{3}H-bungarotoxinbinding, tested as described in the specification (see WO 2004/016608. pages 24-25).